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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,496	10/03/2003	Milan S. Blake	38777-0059	4551

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/677,496	BLAKE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 29-34 are pending and under consideration. In the prior action, mailed on November 30, 2004, claims 1-28 were pending. In the action, claims 1-6 and 10 were under consideration and rejected; and claims 7-9 and 11-28 were withdrawn as to non-elected inventions. In the Response of March 29, 2005, the Applicant cancelled claims 1-28, and added new claims 29-34.

Priority

2. **(Prior Objection- Withdrawn)** Applicants claim for priority to prior application 09/825,770 and 60/194,482 is noted. In view of the amendments to the specification, objections to the reference to priority applications are withdrawn.

Specification

3. **(New Objection-Necessitated by Amendment)** The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not provide antecedent basis for the presently claimed method of producing pertussis toxin comprising the cultivation of B. pertussis both 1) in the presence of a reduced concentration of cysteine, and 2) in the presence of a metal salt such as those identified in claim 29. While the disclosure provides support for either 1) or 2) separately (pages 3-4), and the originally filed claims provide support for the combination of 1) and 2) (see e.g., claims 1, 5, 6, and 11), the

description does not provide antecedent basis support for the presently claimed combination of 1) and 2). It is suggested that the specification (e.g. the summary of the invention) be amended to insert such antecedent basis support.

Note- this is not a rejection for lack of written description because support for the claimed invention is found in the claims as originally filed.

Claim Objections

4. **(Prior Objection- Maintained)** Claim 2 was objected to because of the following informalities: the claim provides a list of alternative members, but does not include a comma separating the last and next to last members. While claim 2 has been cancelled, the same problem is found in the list of salts in line 6 of claim 29 (i.e. no comma between Ag(II) and Ba(II)).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(Prior Rejection- Withdrawn)** Claims 1-6 and 10 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claims read on methods involving "reduced" concentrations of indicated compounds. The term "reduced" is a relative term which renders the claim indefinite. In view of the cancellation of the term from the claims, the rejection is withdrawn.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(New Rejection-Necessitated by Amendment)** Claims 29-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These newly added claims include the limitation "wherein the reduced concentration is no more than 0.05 grams of cysteine per liter." However, while the application disclosed a culture medium comprising 0.05 g/l of a cysteine formulation (see page 12), as well as media containing either 0.04 or .1 g/l (pages 10 and 17), the application nowhere provides support for 0.05 g/l as an endpoint for a range of cysteine concentrations used in a culture media. Thus, there is no written description support for the indicated limitation. The newly added claims therefore add new matter to the claimed methods.

9. **(Prior Rejection- Withdrawn)** Claims 1-6 and 10 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims were rejected as failing to provide adequate written description support for claims drawn to a genus of enhancing the production of 1) any bacterial toxin through 2) culturing the bacteria in a media deficient in any metabolic precursor of 3) any toxin expression inhibitor. In view of the

cancellation of these claims, and the limitation of the present claims to a specific bacterial toxin and a specific precursor of a specific expression inhibitor, the rejection is withdrawn.

10. **(Prior Rejection- Withdrawn)** Claims 1-6, and 10 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of enhancing the production of the PT toxin comprising cultivation of B. pertussis in a cysteine deficient media, does not reasonably provide enablement for methods of enhancing the expression of any bacterial toxin through the cultivation of the bacteria in a media wherein the presence of any toxin expression inhibitor has been eliminated or reduced, or for enhancing the production of any toxin wherein the media is deficient for sulfate ion metabolic precursors. In view of the cancellation of the rejected claims, and the limitation of the present claims to a specific bacterial toxin and a specific precursor of a specific expression inhibitor, the rejection is withdrawn.

11. **(Prior Rejection- Maintained)** Claims 1-6 and 10 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of enhancing the production of PT by culturing B. pertussis in a culture media comprising a reduced concentration of cysteine, does not reasonably provide enablement for methods wherein the culture media is deficient in cysteine. The claims were rejected because the application is not enabling for methods wherein the culture media is deficient in cysteine (i.e. no cysteine present). The rejection is withdrawn from cancelled claims 1-6 and 10, but extended and maintained against new claims 29-34.

While the previously rejected claims have been cancelled, the presently pending claims read on methods comprising no more than 0.05 g/l of cysteine, without providing a minimum

required level of cysteine. Thus, the claims do not require that cysteine be present. Nor does the application provide any indication as to what the minimum required level of cysteine for bacterial growth and PT production is. Because the art teaches that some level of cysteine is required for PT production, and because the present claims do not require the presence of some form and level of cysteine in the growth media, the new claims do not avoid the rejection applied against prior claims 1-6 and 10. The rejection is therefore maintained.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. **(Prior Rejection- Withdrawn)** Claims 1, 5, 6, and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Karlsson et al., Infection and Immunity, 68: 5881-88. In view of the cancellation of these claims, and the restriction of the pending claims to production of pertussis toxin, the rejection is withdrawn.

14. **(Prior Rejection- Withdrawn)** Claims 1-5 were rejected under 35 U.S.C. 102(b) as being anticipated by either of Quentin-Millet et al. (U.S. Patent 4,965,205), or Sekura et al. (U.S. Patent 5,338,670). The Applicant has cancelled claims 1-5, and added new claims 29-34. The

new claims require that the cysteine be present in the culture media at a concentration of no more that 0.05 g/l, and that the media also comprises a metal salt selected from Pb(II), Sr(II), Ag(II), and Ba(II). Although Quentin-Millet teaches the use of a culture media comprising a metal and less than 0.05 g/l of cysteine (see column 3, lines 45-60), the reference does not teach the use of any of the metal salts listed in claim 29. Sekura teaches neither the correct concentrations of cysteine, nor the indicated metal salts. The rejection is therefore withdrawn.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. **(Prior Rejection- Maintained)** Claims 1-5 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,686,180. These claims have been cancelled, and replaced with new claims 29-34. The rejection is withdrawn from claims 1-5 as moot, but extended to new claims 29-34. These claims represent obvious variants of the claims of the prior patent. The claims of the prior patent are generic to the present claims. Further, the particular embodiments described in the present claims are disclosed in those portions of the patent providing support for the claimed inventions.

See, e.g. claims 1, 5,6, 11 of the originally filed application from which the patent issued. Additionally, it would also have been obvious to those in the art to combine the method in the claims with the other methods disclosed in the patent for the production of PT. See e.g., MPEP § 2144.06 (Combining equivalent known for same purpose). Because the present claims are directed to an obvious variation of the methods claimed by the patent, the rejection is maintained over newly added claims 29-34.

17. The above rejection is, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804 II (B)(1):

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 4/16/05
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